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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/552,133

10/06/2005

Lars-Goran Wistrand

PN0335

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06/07/2010

GE HEALTHCARE, INC.

IP DEPARTMENT 101 CARNEGIE CENTER

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EXAMINER

PERREIRA, MELISSA JEAN

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

06/07/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/552,133	<b>Applicant(s)</b> WISTRAND, LARS-GORAN	
	<b>Examiner</b> MELISSA PERREIRA	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 13-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/14/10 has been entered.
2. Claims 13-22 are pending in the application.

### ***Response to Arguments***

3. Applicant's arguments with respect to claims 13-22 have been considered but are moot in view of the new ground(s) of rejection.

### ***New Grounds of Rejection Necessitated by the Amendment***

#### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 13,17 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Jørgensen et al. (US 5,599,522) as evidenced by Ardenkjaer-Larsen (US 6,108,574).

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6. Jørgensen et al. (US 5,599,522) teaches of ESREMRI of the triarylmethyl radical,  $\bullet\text{C}(\text{Ar}^1)_3$ , where Ar is thienyl, phenyl, etc. (column 4, lines 14+). The triarylmethyl radical is generated from the precursors, such as  $(\text{Ar}^{12})_3\text{CLv}(\text{Lv})$  (sample) wherein Lv is a displaceable group such as  $(\text{Ar}^{12})_3\text{CHal}$ ;  $(\text{Ar}^{12})_3\text{C.CO.O.O.CO.C}(\text{Ar}^{12})_3$ , etc. and Hal is Br, Cl, etc. (column 10, lines 65+; column 11, lines 1-6 and 18-36). ESREMRI is electron spin resonance enhanced magnetic resonance imaging or Overhauser MRI which involves exposing the sample to a first radiation of a frequency selected to excite nuclear spin transitions in selected nuclei in the sample and also exposing the sample to a second radiation of a frequency selected to excite electron spin transitions coupled to nuclear spin transitions for at least some of the selected nuclei, such as microwave (column 2, lines 1-28). The radicals may be prepared via photochemical reaction and/or reaction with less stable radicals such as tert-butyl peroxide (radical precursor) in a pharmacologically acceptable carrier or excipient (i.e. solvent) (column 11, lines 37+). The radicals, such as tert-butyl peroxide of the disclosure anticipate the radicals of the instant claims and thus have the same properties, such as decomposing to a non-radical species at temperatures from about 5K to about 273K, etc. and are capable of the same functions.
7. Ardenkjaer-Larsen (US 6,108,574) teaches that ESREMRI is a method of dynamic nuclear polarization (column 1, lines 36-49).

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 13-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (*Acc. Chem. Res.* **1969**, 2, 110-114) and Savitsky et al. (*J. Phys. Chem. A* **2000**, 104, 9091-9100) in view of Bao-Lian et al. (*Acta Physica Sinica*, 1998, 7, 106-114) and in further view of Bajaj et al. (*J. Mag. Res.* **2003**, 160, 85-90) and Wikipedia glycerol data page.

10. Fischer et al. (*Acc. Chem. Res.* **1969**, 110-114) discloses that during rapid radical reactions in liquid, the nuclear magnetic resonance spectra of the reacting solutions often show emission and/or enhanced absorption lines which become absorption lines of normal intensities at the end of the reaction and that these effects have been observed during thermal decompositions of organic peroxides and azo compounds (p110, first full paragraph). According to the theory of dynamic nuclear polarization (DNP) the nuclear spin states of free radicals may in fact become populated by relaxations due to magnetic electron-nuclear interactions in such a way that the corresponding NMR transitions show emission or enhanced absorption if the electron spin states of the radicals are equally populated. Further, the explanation required that during radical formation in chemical reactions two radicals with antiparallel electron spins are always generated simultaneously and that nuclei conserve their nuclear spin

states during product formation from radicals. With these assumptions the electron spin states of the radicals are initially equally populated, the populations of the nuclear spin states are then changed by DNP, and the results of this change is subsequently observed in the NMR spectra of the product molecules (p110, third full paragraph).

11. According to this qualitative picture the effect of NMR emission and/or enhanced absorption during radical reactions is closely related to the physical effect of DNP, it has been named chemically induced dynamic nuclear polarization (CIDNP). The similar and related effect of optionally induced dynamic nuclear polarization of molecules in the solid state and in solution arise from DNP in their triplet states has also recently been discovered (p110, fourth full paragraph).

12. Fischer et al. further discloses experimental results on CIDNP during thermal decomposition of peroxides and azo compounds. Solutions of peroxides and azo compounds were prepared at room temperature and transferred to the preheated probe of the NMR spectrometer and the spectra recorded repeatedly (p110, fourth full paragraph; results). Figure 1 shows the NMR spectra during the decomposition of dibenzoyl peroxide (BPO) at 100° in cyclohexanone (solvent/NMR active material). At  $t = 0$  only the normal absorption lines of the BPO protons are observed. During the reaction the BPO lines vanish and an emission line appears, decreases and reappears in absorption (p111, paragraph 1; figure 1).

13. The features of CIDNP also hold for the NMR spectra of products of azo compound decompositions wherein azobis(isobutyronitrile) (AIBN) decomposes at 100° in tetrachloroethane (solvent/NMR active material) (p112, second full paragraph).

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14. Fischer et al. does not disclose the radical generation via photolysis.
15. Savitsky et al. (*J. Phys. Chem. A* **2000**, *104*, 9091-9100) discloses the CIDEP examination of the generation of transient 2-cyano-2-propyl radicals by laser flash photolysis of AIBN (2,2'-azobisisobutyronitrile) in solvents of various viscosities, such as benzene, ethyl benzoate, di-n-butyl phthalate, etc. (i.e. NMR active material) (abstract; p9092, 2. Experimental Section and 3. Analysis of EPR-Time Profiles).
16. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize laser flash photolysis of AIBN for the preparation of free radicals for the examination of the CIDEP as both disclosures are drawn to the same radical species generation (AIBN) for the examination of CIDEP.
17. The radicals of the disclosure encompass the radicals of the instant claims and thus have the same properties and are capable of the same functions, such as decomposing to a non-radical species at temperatures from about 5K to about 273K, etc.
18. The combined references of Fischer et al. and Savitsky et al. do not disclose the use of DNP comprising simultaneous microwave irradiation.
19. Bao-Lian et al. (*Acta Physica Sinica*, 1998, *7*, 106-114) discloses that dynamic nuclear polarization (DNP) is an electron-nucleus double magnetic resonance technique which can enhance the nuclear polarization by one to three orders of magnitudes during simultaneous microwave irradiation at or near the electron Larmor frequency. It is a powerful means of increasing detective sensitivity of nuclear magnetic resonance

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(NMR) and acquiring information regarding structures and dynamics of the local electrons in solution and solids which contain free radicals. DNP methods have been successfully combined with high-resolution solid state NMR technique (p106, I. Introduction).

20. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize the DNP technique of Bao-Lian et al. comprising simultaneous microwave irradiation for the enhancement/increasing detective sensitivity of the NMR spectra during radical formation of Fischer et al. (via thermal decomposition) or Savitsky et al. (via laser flash photolysis) as Bao-Lian et al. teaches that the techniques are advantageously used concurrently to provide information regarding structure and dynamics of the local electrons of free radicals found in solutions or solids.

21. The combined references of Fischer et al. and Savitsky et al. do not disclose a mixture frozen in liquid nitrogen.

22. Bajaj et al. (*J. Mag. Res.* **2003**, 160, 85-90) discloses that solid state multidimensional NMR techniques used for the examination of biological systems is limited due to the low sensitivity of solid state NMR (p85, Introduction paragraph 2; p86, paragraph 1). Therefore, Bajaj et al. teaches of the enhancement of nuclear spin polarization by DNP with microwave irradiation in static and spinning solids, such as the DNP examination of 1-<sup>13</sup>C-glycine dispersed in a frozen 60:40 glycerol/water matrix with a nitroxide radical 4-amino-TEMPO as the paramagnetic dopant (abstract; p86, paragraph; p87, 4. DNP CP of Static samples; p88, 6. Conclusion; figure 3). Bajaj et al.

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also discloses DNP examination of U-<sup>13</sup>C, <sup>15</sup>N-proline in a 60% glycerol matrix doped with TEMPO via microwave irradiation (p88, 5. DNP MAS experiments at 9T).

23. Wikipedia glycerol data page discloses that a 60% glycerol solution freezes at 33.6°C.

24. Bajaj et al. teaches that freezing of the DNP samples is sufficiently rapid (Bajaj et al. p87, 4. DNP CP of static samples). Therefore, at the time of the invention it would have been obvious to one ordinarily skilled in the art to freeze a 60% glycerol solution which freezes at -33.6°C, as taught by wikipedia glycerol data page, with liquid nitrogen as it is well known in the art that liquid nitrogen can instantaneously supply a freezing temperature sufficient to cause rapid freezing of a 60% glycerol solution.

25. Bao-Lian et al. teaches that DNP is used to examine solids which contain free radicals and Bajaj et al. teaches that DNP can be used to overcome the low sensitivity of solid state NMR for biological systems. Therefore, at the time of the invention it would have been obvious to one ordinarily skilled in the art to freeze a sample containing free radicals according to the disclosure of Bajaj et al. depending on the sample desired for observation, such as for the study of biological systems via DNP and thus overcome the low sensitivity of solid state NMR/provide information regarding structure and dynamics of the local electrons of free radicals of the desired biological systems.

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26. Claims 13,17 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jørgensen et al. (US 5,599,522) in view of Ardenkjaer-Larsen (US 6,108,574).

27. Jørgensen et al. (US 5,599,522) teaches of ESREMRI of triarylmethyl radical,  $\bullet\text{C}(\text{Ar}^1)_3$ , where Ar is thienyl, phenyl, etc. (column 4, lines 14+). The triarylmethyl radical is generated from radical precursors, such as  $(\text{Ar}^{12})_3\text{CLv}(\text{Lv})$  (sample) wherein Lv is a displaceable group such as  $(\text{Ar}^{12})_3\text{CHal}$ ;  $(\text{Ar}^{12})_3\text{C.CO.O.O.CO.C}(\text{Ar}^{12})_3$ , etc. where Hal is Br, Cl, etc. (column 10, lines 65+; column 11, lines 1-6 and 18-36). ESREMRI is electron spin resonance enhanced magnetic resonance imaging or Overhauser MRI which involves exposing the sample to a first radiation of a frequency selected to excite nuclear spin transitions in selected nuclei in the sample and also exposing the sample to a second radiation of a frequency selected to excite electron spin transitions coupled to nuclear spin transitions for at least some of the selected nuclei, such as microwave (column 2, lines 1-28). The radicals may be prepared via photochemical reaction and/or reaction with less stable radicals such as tert-butyl peroxide (radical precursor) in a pharmacologically acceptable carrier or excipient (i.e. solvent) (column 11, lines 37+). The radicals, such as tert-butyl peroxide of the disclosure encompass the radicals of the instant claims and thus have the same properties, such as decomposing to a non-radical species at temperatures from about 5K to about 273K, etc. and are capable of the same functions.

28. Jørgensen et al. does not explicitly disclose that ESREMRI is dynamic nuclear polarization.

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29. Ardenkjaer-Larsen (US 6,108,574) discloses that ESREMRI is a method of dynamic nuclear polarization (column 1, lines 36-49).

30. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the ESREMRI method of Jørgensen et al. is dynamic nuclear polarization as Ardenkjaer-Larsen teaches that ESREMRI is a method of dynamic nuclear polarization and Jørgensen et al. further teaches that the ESREMRI involves the application of microwave to the sample which encompasses the dynamic nuclear polarization method of the instant claims which involves the application of microwave to the sample of interest.

### ***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/  
Examiner, Art Unit 1618